A matrix micropatterning platform for cell localization and stem cell fate determination.

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Public Summary:
To study the role of cell-extracellular matrix (ECM) interactions, microscale approaches provide the potential to perform high throughput assessment of the effect of the ECM microenvironment on cellular function and phenotype. Using a microscale direct writing (MDW) technique, we characterized the generation of multicomponent ECM microarrays for cellular micropatterning, localization and stem cell fate determination. ECMs and other biomolecules of various geometries and sizes were printed onto epoxide-modified glass substrates to evaluate cell attachment by human endothelial cells. The endothelial cells displayed strong preferential attachment to the ECM patterned regions and aligned their cytoskeleton along the direction of the micropatterns. We next generated ECM microarrays that contained one or more ECM components (namely gelatin, collagen IV and fibronectin) and then cultured murine embryonic stem cell (ESCs) on the microarrays. The ESCs selectively attached to the micropatterned features and expressed markers associated with a pluripotent phenotype, such as E-cadherin and alkaline phosphatase, when maintained in growth medium containing leukemia inhibitory factor. In the presence of the soluble factors retinoic acid and bone morphogenetic protein-4 the ESCs differentiated towards the ectodermal lineage on the ECM microarray with differential ECM effects. The ESCs cultured on gelatin showed significantly higher levels of pan cytokeratin expression, when compared with cells cultured on collagen IV or fibronectin, suggesting that gelatin preferentially promotes ectodermal differentiation. In summary, our results demonstrate that MDW is a versatile approach to print ECMs of diverse geometries and compositions onto surfaces, and it is amenable to the generation of multicomponent ECM microarrays for stem cell fate determination.

Scientific Abstract:
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